REMARKS

Examination of claims 1-27 is reported in the present Office action. Claims 1-8, 11-14, 16, and 18-27 were rejected under 35 U.S.C. § 102(b), and claims 1-10 and 13-27 were rejected under 35 U.S.C. § 103(a). Claims 3, 22, 23, and 25-27 were also rejected under 35 U.S.C. §.112, second paragraph. Each of the rejections is addressed below.

Rejections under 35 U.S.C. § 102(b)

Claims 1-8, 13, 14, 16, and 18-27 were rejected under § 102(b) as being anticipated by Dyer et al. (J. Virol. 71:191-198, 1997). Claim 1, from which the other rejected claims depend, has now been amended to recite a method for introducing a virus into a cell *in vivo*. Dyer, which describes *in vitro* studies characterizing the effects of dextran sulfate on HSV infection of glycosaminoglycan-deficient cells, does not describe such *in vivo* methods. Applicants thus respectfully request that this rejection be withdrawn.

Claims 1-5, 11-13, and 19-27 were rejected under § 102(b) as being anticipated by Wu. Wu describes methods for targeting polynucleotides to cells in complexes that also include a polynucleotide binding agent and a bacterial component that has the ability to lyse endosomes. Wu does not describe the introduction of viruses into cells, as is required by the amended claims. Applicants thus respectfully request that this rejection also be withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claims 1-10 and 13-27 were rejected under § 103(a) for obviousness over Dyer, in view of Marasco (U.S. Patent No. 6,143,520) and Mislick (U.S. Patent No. 5,783,566). This rejection is respectfully traversed.

As is noted above, claim 1, from which the other rejected claims depend, has been amended to specify a method of introducing a virus into a cell *in vivo* by contacting the cell with a virus and a charged compound that facilitates uptake of the virus by the cell.

Dyer, as is noted above, does not describe *in vivo* methods. Dyer also does not provide motivation to carry out *in vivo* methods and, in fact, teaches away from such methods. In particular, the focus of Dyer is characterization of the contribution of cell surface components to the Herpes simplex virus (HSV) infection pathway. Central to Dyer's study is the use of a mutant cell line, sog9, which does not produce glycosaminoglycans (GAGs), the natural cell surface receptors for HSV. Dyer found that exogenously added dextran sulfate enhanced infection of sog9 cells by HSV-1, but not HSV-2, leading to the conclusion that it was the absence of endogenous GAGs in these cells that enabled the identification of this difference between HSV-1 and HSV-2 (page 197, lines 28-29). Dyer did not suggest the use of dextran sulfate to enhance infectivity *in vivo*, which is not surprising, given that Dyer's results were obtained using mutant cells that do not occur *in vivo*, and that it was only because of the fact that such mutant cells were used that Dyer was able to detect enhanced infectivity. Moreover, regarding the use of dextran sulfate to enhance infection of non-mutant cells, Dyer stated that it was well established that dextran sulfate normally inhibits infection of such cells by enveloped viruses (page 197, lines 1-6). Dyer thus teaches away from the presently claimed invention.

Mislick does not make up for the deficiencies of Dyer in supporting this rejection. Rather, Mislick further teaches away from the use of exogenous glycosaminoglycans to enhance viral infectivity *in vivo*. On this point, Mislick states:

> When transfection is performed *in vivo*, glycosaminoglycans and other polyanionic species in the plasma can adversely affect the transfection efficiency. Transfection efficiency can be increased

by lowering the plasma concentration of glycosaminoglycans...
(column 6, lines 5-9; emphasis added).

Thus, based on the teachings of Mislick, those of skill in this art would seek to decrease, rather than supplement, exogenous glycosaminoglycan concentration if desiring to introduce viruses into cells *in vivo*.

Marasco also does not provide support for this rejection. This reference, which describes the use of lentivirus vectors, such as HIV vectors, for use in gene expression studies, nowhere suggests or provides motivation to enhance viral infectivity *in vivo* by use of a charged compound, such as dextran sulfate.

Thus, because none of the cited references, alone or in combination, suggests or provides motivation to enhance viral entry into cells *in vivo* by the use of a charged compound, which is required by the present claims, applicants respectfully request that the rejection under § 103(a) be withdrawn.

Rejection under 35 U.S.C. § 112

Claims 3, 22, 23, and 25-27 were rejected under § 112, second paragraph for indefiniteness because claim 3, from which the other rejected claims depend, depends from itself. This rejection can now be withdrawn, as claim 3 has been amended to depend from claim 1.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is requested. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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1. (Amended) A method for introducing a virus [nucleic acid vector] into a [living] cell *in vivo*, said method comprising contacting said cell with said virus [vector] and [, either before, during, or after contacting said cell with said vector, contacting said cell with a liquid medium comprising] a charged compound that [, in said medium, is charged, non-cytotoxic, and capable of facilitating the] facilitates uptake of the virus [vector] by the cell.

3. (Amended) The method of claim [3] 2, wherein said mammal is a human patient.

4. (Amended) The method of claim 1, wherein said virus [vector] comprises [a] an exogenous gene encoding a [polypeptide, a hormone, a vaccine antigen, an antisense molecule, or a ribozyme] therapeutic product.

5. (Amended) The method of claim 4, wherein said therapeutic product [polypeptide] is selected from the group consisting of hormones, vaccine antigens, antisense molecules, ribozymes, growth factors, enzymes, anti-angiogenic polypeptides, and polypeptides that promote cell death.

7. (Amended) The method of claim 1 [6], wherein said virus [vector] is selected from the group consisting of Herpes viruses [a Herpesviridae], Dengue viruses, Adeno-associated viruses [virus], Adenoviruses [Adenovirus], papillomaviruses [papillomavirus], and retroviruses [retrovirus based vectors].

8. (Amended) The method of claim 7, wherein said Herpes virus [vector] is selected from the group consisting of HSV-1, HSV-2, VZV, CMV, EBV, HHV6, HHV7, and HHV8.

9. (Amended) The method of claim 7, wherein said virus [vector] is a lentivirus [-based vector].

10. (Amended) The method of claim 9, wherein said virus [vector] is a human immunodeficiency virus [an HIV-based vector].

13. (Amended) The method of claim 1, wherein said virus [vector] is attenuated.

14. (Amended) The method of claim 1, wherein said charged compound [molecule] is selected from the group consisting of charged polysaccharides, polylysine, acyclodextrin, diethylaminoethane, and polyethylene glycol.

19. (Amended) The method of claim 1, wherein said charged compound [molecule] is contacted with [administered to] said cell prior to [the administration of] said virus [vector to said cell].

20. (Amended) The method of claim 1, wherein said charged compound [molecule] is contacted with [administered to] said cell concurrently [concurrent] with [the administration of] said virus [vector to said cell].

26. (Amended) The method of claim 3, wherein said virus [vector] and charged molecule are delivered locally to said patient.

27. (Amended) The method of claim 3, wherein said virus [vector] and charged molecule are delivered [delivery] systemically to said patient.